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## WHAT IS LIFE?

LECTURE DELIVERED AT CLARK UNIVERSITY.

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Not many years since tradition would have had a ready answer to this question. The whole Middle Ages is characterized by the tradition that life is a process caused in the body by the soul, or, in other words, by a living power. It was something supernatural that caused life, something eluding investigation, not subordinate to the laws of nature. In the meantime, mankind has been forced from this attitude toward the problem of life by necessity,—necessity, that is, the sufferings of mankind and the desire to heal or, at least to ameliorate them. Out of this sympathy and the wish to heal disease medical science has arisen. It first began by collecting facts concerning everything known that would alleviate pain, but, in proportion as this store of experience grew, in proportion as the attempt was made to systematize this knowledge, in other words in proportion as the art of healing began to be taught as a science, it was no longer possible to ignore the fact that disease is a change in the processes of life, and that it was only possible to recognize the changes when it was known what had been changed, that is, what life is. Thus, Physiology, the study of life, came to form the foundation of medical science. This Physiology has already developed some conceptions of life as a scientifically recognizable process. It is in these conceptions of life that I wish to introduce certain modifications and it is of these that I wish to speak to you today. My modifications are dictated by the apprehension that the now prevalent ideas concerning the phenomena of life

will not lead us to the point where we can obtain the desired knowledge of the condition of living organisms. They cannot form the basis of medical science because they do not represent the reality.

There is, for instance, the conception you will find incorporated in most text books of physiology that living organisms are comparable to machines. Just as the machine develops energy out of the materials furnished and converts it into work, so does the living being. At the last Physiological Congress in Turin I protested against this conception, and called attention to the fact that an essential difference between the machine and the living being consists in the fact that in the former the structure remains unchanged whereas in the latter the structure, that is, the body, changes. All experience, especially that of the physiologists, indicates that the difference between the machine and the living being is, that the former converts the calorics of combustible materials directly into energy; the latter, on the contrary, first makes the food a part of the body, while the tissues of the body in their turn decompose into simpler combinations thus developing energy. In a certain sense life consists of two processes, a constructive and a destructive, a truth that first occurred to Claude Bernard who says, "la vie c'est la création et la mort.

Connected with this is a second modification of opinion that I would suggest. You will frequently find the living organism compared to a state consisting of cells in which every individual cell carries on a separate independent existence, takes its nourishment from the common store according to its need, and converts the calorics of the same into energy in compliance with its own organization. I do not admit that the cells are independent of one another. It is not so much that the term "Zellen Staat" is misleading, for in the state individuals are not so independent of one another as appears at first thought. It is the inferences that have been drawn from this term that make it misleading. Each cell, like each individual, has been considered equal to the others in respect to its food. Just as each individual needs a certain amount of carbohydrates, proteids and fats, so each cell takes its carbohydrates, proteids and fats from the supply in the blood and changes them into the final products of the metabolic processes. This is, in my opinion, a false inference. Each cell requires for the work it has to accomplish and, what amounts to the same thing, for the maintenance of its structure quite specific substances. They receive these substances from the other cells that have produced them through the medium of the blood or the nerves. The whole organism resembles a chemical laboratory with as many apartments as there are organs or glands.

The substances produced in each apartment are those needed in others either for their construction or for their work. I first had occasion to convince myself of this dependence of one organ upon another in a series of experiments to which I gave the name Experiments in the Trophic Functions in accordance with the usage of other investigators.

Fig. 1 shows what occurs in the *Biceps* and *Psoas* of the rabbit after the *ganglion cervicis infimum nervi symphatici* has been irritated. At *a a* a number of the muscular fibers have been changed while others near by are normal. These muscular fibers are torn and larger than the normal fibers, their contents have disintegrated into lumps and are stained dark with haematoxylin, while the normal fibers are red with eosin. Immediately after the experiment, the former fibers seem to be laden with a white inorganic substance that stands out distinctly against the red bottom of the groove lying between the two ends of the muscle. In the groove one sees swollen blood vessels, blood outside the blood vessels and numerous connective tissue cells and nerves. The only explanation that I could find at first for such a change in the tissues was, there were certain substances necessary for the normal construction of the muscle and that, in consequence of the irritation of the ganglion, it was receiving either too much or too ltttle of the one or the other. Either the nerves or the blood vessels must have brought them here, the fact that the nerves showed changes in their structure spoke for the one hypothesis. Or the muscles may have received their materials from the blood and only the capacity to assimilate them from the nerve is lost, it acting in the character of a ferment. The swollen blood vessels and the circumstance that the alteration occurred subsequent to the irritation of the *ganglion symphatici*, that, as we know, contains the nerves of the blood vessels, seemed to favor the latter hypothesis.

All cells are dependent upon substances produced by other cells for their building material. Whether the nerves or the blood form the means of transit by which producers and consumers are connected, they form a unit. If the place of production is destroyed, or if the means of connection is interrupted, the consumer is also affected.

But my trophic investigations not only led me to a knowledge of this unity, but through them I gradually came to realize that the organism is in a state of ceaseless inner change quite independent of the experiments one makes upon it, or the special surroundings and conditions under which one observes it. Allow me to put this down as the third point in the change of front that I suggest, and to formulate it thus: Life is a continual change of the organism, that is influenced in-

deed by its surroundings but is not directly called forth by them. I gained this insight in the following way. While I was making test experiments to control the above mentioned observations, I made preparations of the muscles of animals that had in no way been operated upon and had been killed with chloroform. I discovered here similar changes to those in the operated animals. To be sure the changes were much less extensive than those in the operated animals, thus betraying the influence of the experiment, but what could call forth such changes in a normal animal? The first thought was, perhaps, that these are not changes but peculiarities of the muscles, but further investigation proved that at other times the muscles show none of these changes and were like those we consider normal. Thus there are changes, changes called forth by an experiment on the *nervus symphaticus* but that may also occur in the muscles of a normal animal, where no experiment has been made. I had to ask myself what these changes could signify? Then I observed some peculiar places in the skin-muscles of some rabbits that had not been operated upon. Microscopic investigation showed changes in the muscular fibers, in the blood vessels, in the connective tissue and in the nerves similar to those I had already seen in the *Biceps* and *Psoas* and have described above. These changes, however, were more circumscribed and much less extensive than those after an experiment. Their size is generally that of a pea. Fig. 2 is the photograph of such a change. The muscular fibers are torn for about 5 m. m., and the thickened ends, filled with coagulated matter, surround the intervening depression like a wall. Imbedded in the wall is the white substance already mentioned, that becomes whiter when treated with oxalic acid and dissolves in hydrochloric acid, thus indicating the presence of some lime compound. A medullated nerve is always to be found passing through the hollow and when the preparation is treated with perosmic acid, the nerve outside the groove is found to be stained black as usual. This medullated nerve, however, loses its affinity for perosmic acid at at least one point in the groove and during the remainder of its course therein it resembles a degenerated nerve. The white substance or myelin consists of blackened granules in the segments or cells as in Fig. 2. The blood vessels in the hollow are very remarkable. One finds regularly such an object as that at Fig. 2, b, namely a vein, to judge from the character of the walls, that is distended up to a semilunar object that abruptly checks the distension. Such an object is a familiar one to those who have made injections of blood vessels. It occurs when the injected fluid flows backward and is retained by the valves of the vein. Does the blood flow backward here? And what is the

connection between this process and the loss of myelin in the nerve, the tearing of the muscular fibers, the filling of the connective tissue with cells and the precipitation of a substance containing lime? The cause of this was not an experiment, the changes were called forth in the course of the undisturbed inner life of the animal. This can only be the result of a reconstruction taking place in the organism; this reconstructive process is so exaggerated at certain points that the function of the muscle is disturbed. The places are circumscribed so that the general life of the animal is not threatened. They may not affect the animal otherwise than in the form of growing pains that make us uncomfortable in youth. But these places are there; they are irrefutable witnesses of a process going on in the interior of the organism without external incitement. What is this process?

I have studied chiefly the frog for the changes taking place periodically in an organism, and have published the results in my paper "Die Veränderungen des Froschorganismus (*R. esculenta*), während des Jahres." The method by means of which I made these observations was to weigh the single organs and, in order to be independent of the varying size of the frogs, I estimated in each case the relative weight of the organ to the weight of the body. The organism of the frog is especially adapted for these observations because of the hunger period during the winter months. During this time no food is taken and a minimum of work is done, thus, if during this period the relative weights of the organs to one another vary, this can only happen by one organ losing while another gains, that is, one organ is reconstructed at the expense of another or from the material stored in another. The curves constructed on the basis of these observations and published in the above mentioned paper show that the relative weight of the sexual organs increases during the fasting period. This can only occur at the expense of the other organs and the reconstruction of the cells of organs into sexual products must take place within the living frog, during the hunger period, at a time when no external influence is affecting it and when it is quite oblivious to its surroundings. Miescher showed that the muscles of the salmon supply the materials for the sexual products. I further weighed the muscles of rabbits and found that their weight alternately increases and decreases. A report of these investigations was given at the Physiological Congress in Bern. On weighing the testes of the rabbit in the same way, I found similar variations of weight, betraying a similar relation of muscles to sexual products in the rabbit as in the salmon. The weight curve of the M. *gastrocnemius* of *R. esculenta* reproduced in the above mentioned paper disclosed a change here

also during the period of growth of the sexual organs. Now the second point in the reforms suggested leads one to think that it is not two organs only that are involved in this reconstruction. It is not simply that one organ supplies the material from which the other builds its cells. The whole organism is a unit, the life process is a unit, hence if one organ is changed all the others must change also, if sexual products are being formed then the whole organism must reconstruct itself. Hence it is that the curves of all the organs investigated of the frog also show a change in the relative weights in the course of the sexual period, that is, of the year. This is chiefly evident in the liver curves, the most important and largest organ of metabolism. The differences between the livers of the two sexes in the frog (*R. esculenta*) show what part the sexual organs play in this metabolism.

In the further course of this study of the changes in the organism that occur in connection with the reconstruction of the cells of the organs and the construction of the sexual products, I noticed something that seemed at first quite unexplainable. A more careful inspection of the curves makes it obvious that the growth of the sexual products is not continuous. The curves of the ovaries descend in March, those of the oviducts and the testes in February. The curves of the liver and the muscles on the contrary ascend in February. The opposite of what we found taking place in the other months occurs here, the sexual organs are not developed at the expense of the other organs but these at the cost of the sexual organs.

Now within two days in the month of February this year I discovered 10 frogs (*R. esculenta*), 9 females and 1 male, that had either none or very small sexual organs and this was the case without exception with all the frogs I examined during these two days. At the same time there was an exceptional increase in the size of the liver. Again, the difference in sex was especially noticeable in these enlarged livers.

Figs. 3 and 4 are photographs of microscopic preparations of these livers, the one of the male the other of the female frog in which the sexual products had so far disappeared that it was difficult to find the place where they had been attached. One sees a marked difference in them. In Fig. 3 the liver contains large groups of cells between the tubuli, and in Fig. 4 it contains nothing of the kind. On the other hand the liver cells themselves in Fig. 4 are much larger and occasionally there are small clumps of pigment cells between them. The large groups of cells characteristic of the female liver betray some connection with the blood, for they contain red blood corpuscles at various stages of development. Thus when testes and ova-

ries lose material, both deliver it to the same organ. The differences in the sexual structures disappear so far as concerns the individual. Yet the substances from the male and female organs evidently play a different part in the metabolism of the liver, the material of the ovaries passing into special groups of cells in which it is probably transformed into blood, the material of the testes into liver cells. Both materials pass into cellular elements of the producing organism but not into the same kind. I give these two illustrations because they show very distinctly the connection between the sexual and the individual structures, but not only on this account. The restless mill of change through which the organism is continually passing under the influence of cosmic forces finds its illustration here. What is happening here on a large scale is constantly occurring in the organism on a smaller one. How can such an inversion of processes take place in the organism? The fact of such an inversion we must accept for the curves show that before and after this period the sexual products are built up at the cost of the rest of the body and I could complement these curves with innumerable observations made in the course of other work. Something must happen just at this time in the month of February that causes an inversion of the processes going on before and after. This something influences the whole month of February as the curves for this month prove, but it is most evident on certain days to which those belong in which I studied the frogs this year. What can this something be? I expected that the whole sexual period, the maturing of the sexual products from one spawning to the next, was coincident with the cosmic period, the year. I discovered in other cases the coincidence of living processes with a cosmic period. At certain times the fat bodies of *R. esculenta* disappear during the night and are rebuilt during the day. This is an adaptation to the day period.

In Turin I showed how, in my study of the frog's blood, I had found an adaptation to the monthly period in the varying number of the blood corpuscles. How is it possible that the cosmic forces obtain an influence in the formation of the cells of the living organism? This can only be when the forces that cause them, the cosmic forces, also influence the fundamental processes of life. Nor is this very strange. An organism living in the world, must after all to some extent become adjusted to the mightiest forces governing the world.

What are these forces? Heat, light, electricity — their periods probably correspond to the cosmic periods mentioned. Now a living organism is under the influence of all these forces simultaneously. Something that, like the formation of the sexual products, requires an annual period for its

accomplishment, will at the same time pass through the daily and monthly periods. This building up occurs at the expense of the other tissues of the organism. The other tissues also pass through a periodic evolution in which a maximum and minimum are attained. Their periods must therefore have an influence on the formation of the sexual products. Now the periods are marked by the alternate approach of the organ to a maximum or minimum, and when these organs are in contra position to the sexual organs, while the sexual products are growing at their expense, then, when they approach a maximum a falling off in weight will be noticeable in the sexual organs. In most months this falling off will be obscured in the change of influence that the various organs exert over the sexual products. But the curves that I published last year at Turin concerning the number of blood corpuscles show that the monthly variations are very different in size, that is, the influence of the cosmic force upon the formation of the blood corpuscles is very different in different months. Hence, it is possible that in February a cosmic force of monthly periodicity may obtain such an influence over the organism of the frog that the sexual organs decrease while other organs, above all the liver, increases.

Hence the condition of the organism is at every moment dependent upon the cosmic forces affecting it, the mill of change that destroys cells and builds new ones is unceasingly active. Only when we have come to know the periods of the cosmic forces and their exact influence, can we say, that we may expect to see this or that in an organ. But are there not such representations of organs made without this knowledge? The text books of Anatomy, Histology and Physiology and other sciences represent and describe these organs as if they were unchangeable and of a quite definite structure. The most exact copy of a preparation of an organ can only possess the value of an instantaneous photograph of a transitory condition. Then one must remember that those that give these illustrations are not only photographers but also investigators. Among all the details the investigator selects the prominent and most frequently recurring features and the pictures they give are, to a certain extent, the *résumé* of a number of conditions.

Now I come to the last point to which I wish to call attention. Life in the living being is a continual process of reconstruction. In doing this it adapts this being to the world, it takes place under the influence of the cosmic forces. But to sustain life it must adapt the living being to its environment. Science has concerned itself until now almost wholly with this adaptation. This can only take place in the recurrence of the

secondary wave on the primary wave crest but it must also lead to a re-formation of the living being, if the propositions I have suggested are to be useful. Can we perceive anything of this re-formation? At present, and as long as the reconstruction under the influence of the cosmic forces is so little known, we can detect it only when the change of environment is great and very rapid. Then the inner change will be so significant that we can attribute it only to the change of environment. A year ago I was placed under such varied conditions of life that the changes that took place in my blood could be attributed only to these external variations in the surroundings. This was during my balloon ascents. In the first I reached an altitude of 5,300 meters and at 4,700 meters the number of blood corpuscles was counted and the unusual number of 8,800,000 was found. Since my companions also had a very high number of corpuscles I determined on my second ascent to make preparations of my blood in order, if possible, to discover the changes in it that might explain such an increase. The second ascent took us to the altitude of 4,200 meters. The number of my blood corpuscles was somewhat less than before, still 8,080,000 was an enormous increase over the number I had counted only three hours before in my laboratory. Fig. 5 is a photograph of the preparation made of my blood at 4,200 meters. Many of the blood corpuscles up there had nuclei and down below they had none. That the red blood corpuscles of man contain no nuclei has become an axiom of the histologist. These nucleated blood corpuscles throw some light on the manner of increase of the blood corpuscles, for nuclei are an indication of dividing, that is, multiplying cells. It shows us also that the blood adapts itself to the changed conditions in high altitudes by changing its structure, for the cells take the place of the structure of the machine. In so rapid a change we have not to consider a simple development of force between isolated molecules in a solution, no, we have a change taking place in complicated blood corpuscles. Just as the organism adapts itself to the world, the inner mill remodelling the cells under the influence of the cosmic forces, so it also adapts itself to the changed environment, the cells becoming different. We are ever under this double influence. The one process of ceaseless movement, by which the cells of the organism and the sexual products are formed, must combine with the other by which the cells sustain their life and that of the organism in opposition to the forces of the environment. The cells disappear again as quickly as they were formed. After my descent the number of my blood corpuscles was only 5,600,00. Fig. 6 is the photograph of a preparation of my blood then. The nuclei have quite disappeared. This case of adaptation is wonder-

fully instructive. It shows all the difference between the organism and the machine, the latter has to do with the development of power, the former with a change of structure. It also shows us that we are at the beginning of a new period of knowledge in which we shall be obliged to follow the state of the organism in connection with the conditions under which it sustains its life even to the cells. This period introduces new problems, it also promises us new fruits among which—if I overlook the effect upon medical science—I count, as not the least, a new conception of evolution.

## Explanation of Plate.

Fig. 1. Photograph of cross section of a skin muscle with trophic change. The unchanged fibers a a are stained red, those with trophic changes are stained from blue to dark blue and black. Section in Canada balsam.

Fig. 2. Photograph of a trophic change in the skin muscle. The muscle is spread out and treated with $Os\ O_4$ and laid in glycerine. a a The torn and changed fibers form a ridge or wall. b The nerve stained with $Os\ O_4$, b′ point where the medullated sheath is no longer blackened. c The vein, c″ the enlarged vein with the valve.

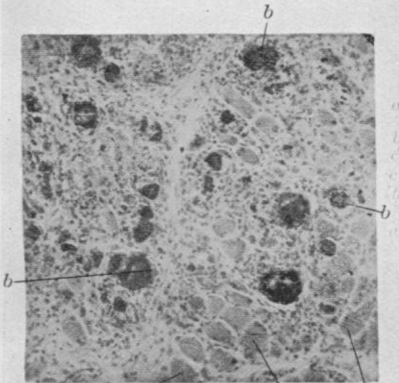
Fig. 3. Photograph of a section of the liver from a *R. esculenta* female after the disappearance of the ovaries. a–a Liver cells. b–b Large groups of cells between the liver cells.

Fig. 4. Photograph of a section of the liver from a *R. esculenta* male after the disappearance of the testes. a–a Liver cells. b–b Small groups of pigment cells.

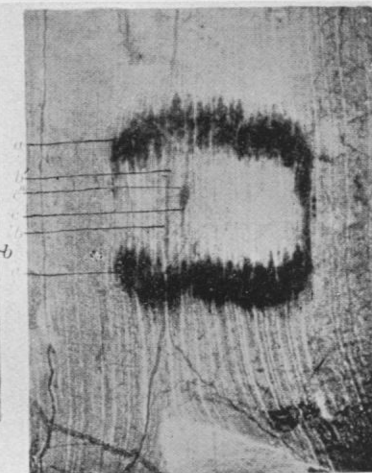
Fig. 5. Photograph of blood at an altitude of 4,200 meters. Blood fixed in the balloon three hours after ascent. The nuclei are dark blue sharply defined spots. In some instances it is a mere point, at others it is larger. Highly magnified.

Fig. 6. Photograph of blood after the return from the balloon ascent. The blood corpuscles are rich in hæmoglobin, are evenly stained and no differentiation is discernible.

As the corpuscles are stained with eosin, which makes little impression on a photographic plate, they appear like shadows.




Photograph 1



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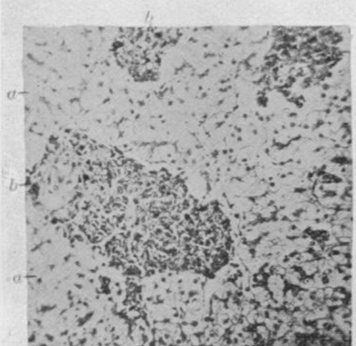


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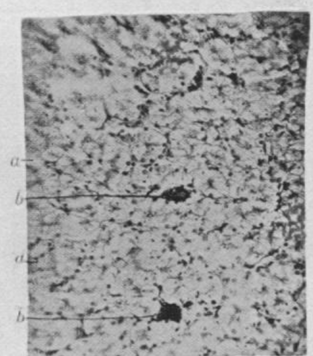


Photograph 4

Photograph 5

Photograph 6